AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior listings of claims in the application:

LISTING OF CLAIMS:

1. (Withdrawn) A method for purification of an EGFR family derived protein, said protein being recombinantly produced in an insect cell culture and said protein being one that is suitable for purification by means of immobilised metal affinity chromatography, the method comprising obtaining, from said insect cell culture, a substantially cell-free sample containing said EGFR family derived protein, and thereafter enriching for said EGFR family derived protein by means of subsequent steps of

diafiltration and exchange of culture medium with buffer, - immobilized metal affinity chromatography (IMAC),

size exclusion chromatography (SEC), and

anion exchange chromatography (AIE).

2. (Withdrawn) The method of claim 1, wherein the EGFR family derived protein includes a heterologous amino acid sequence that facilitates purification by means of IMAC.

3. (Withdrawn) The method of claim 2, wherein the heterologous amino acid sequence is rich in histidine residues.

4. (Withdrawn) The method according to claim 3, wherein the heterologous amino acid sequence comprises residues 1-14 of SEQ ID NO: 2.

5. (Withdrawn) The method according to any one of the preceding claims, wherein the EGFR family derived protein comprises a substantial part of the amino

acid sequence of human EGFR or human HER-2.

6. (Withdrawn) The method according to claim 5, wherein the substantial portion is mainly derived from the extracellular portion of EGFR or HER-2.

7. (Withdrawn) The method according to claim 5 or 6, wherein the EGFR family derived protein is a variant of human HER-2.

8. (Withdrawn) The method according to claim 7, wherein the variant of human HER-2 includes at least one foreign T helper cell epitope.

9. (Withdrawn) The method according to claim 8, wherein the variant of human HER-2 includes tetanus toxoid epitopes P2 (residues 269-282 of SEQ ID NO: 2) and P30 (residues 649-669 of SEQ ID NO: 2).

10. (Withdrawn) The method according to claim 9, wherein the variant of human HER-2 includes amino acid residues 17-677 of SEQ ID NO: 2.

11. (Withdrawn) The method according to claim 10, wherein the amino acid sequence of the variant of human HER-2 consists of residues 1-677 of SEQ ID NO: 2.

12. (Withdrawn) The method according to claim 1, wherein the step of diafiltration/buffer exchange is performed at a temperature from about 2 to about 25°C, preferably at a temperature of about 3 to about 8°C, optionally with the addition of a detergent such as Tween when the temperature is beyond 10°C.

13. (Withdrawn) The method according to claim 12, wherein the diafiltration is performed in two rounds so as to initially concentrate macromolecular compounds in the sample of culture medium and thereafter to exchange culture medium with buffer.

14. (Withdrawn) The method according to claim 13, wherein the macromolecular compounds are concentrated between about 2 and about 25 times.

15. (Withdrawn) The method according to claim 14, wherein the macromolecular compounds are concentrated about 3-5 times.

16. (Withdrawn) The method according to any one of claims 12-15, wherein the buffer exchange is performed in one or two subsequent steps of which the first takes place at a pH of at least 6.5 and at most 7.2 and of which the second optional step takes place at a pH of at least 7.0 and of most 8.0.

17. (Withdrawn) The method according to claim 12, wherein a phosphate buffer is used for the buffer exchange.

18. (Withdrawn) The method according to claim 1, wherein imidazole, histidine or a high salt concentration buffer is added to the diafiltrated and buffer exchanged sample or wherein the buffer exchanged sample is substantially unaltered.

19. (Withdrawn) The method according to claim 18, wherein imidazole, when added, is added to reach a concentration of between about 0.05 to about 20 mM.

20. (Withdrawn) The method according to claim 1, wherein a detergent selected from a Polyoxyethylene sorbitan fatty acid ester, an alkylaryl polyether alcohol, and a carbohydrate based detergent, is added to the diafiltrated and buffer exchanged sample to reach a concentration of between about 0.05% (v/v) and 10% (v/v).

21. (Withdrawn) The method according to claim 1, wherein the IMAC step involves charging of a chromatographic medium with a divalent metal ion prior to

application of the buffer exchanged sample.

22. (Withdrawn) The method according to claim 21, wherein the divalent metal ion is selected from the group consisting of Ni2+, Cu2+, Zn2+, Co2+, and Fe2+.

23. (Withdrawn) The method according to claim 21 or 22, wherein elution of the chromatographic medium is performed by applying imidazole, histidine, a high salt concentration buffer, or a change of pH onto the chromatographic medium.

24. (Withdrawn) The method according to claim 23, wherein elution of the chromatographic medium is performed by applying imidazole in one single step at a concentration between about 50 mM and about 500 mM, or wherein elution is performed by applying histidine in one single step at a concentration between about 20 mM and 400.

25. (Withdrawn) The method according to claim 1, wherein the SEC step involves elution with a phosphate or TRIS buffer or a biological buffer, such as HEPES.

26. (Withdrawn) The method according to claim 25, wherein the pH is maintained at about 7-8.

27. (Withdrawn) The method according to claim 25 or 26, wherein the average pore size of the SEC matrix separates globular protein between 10 kDa and 600 kDa.

28. (Withdrawn) The method according to claim 1, wherein samples containing the EGFR family derived protein obtained from SEC, if necessary, is diluted before the AIE step so as to adjust a phosphate concentration to less than 15

mM.

29. (Withdrawn) The method according to claim 1, wherein the AIE step involves loading of the sample containing the EGFR family derived protein obtained after SEC on a strong or weak anion exchange matrix, or both.

30. (Withdrawn) The method according to claim 29, wherein elution is performed with a buffered NaC1 solution at a pH between 7 and 8.

31. (Withdrawn) The method according to claim 1, wherein a virus inactivation step is introduced between the diafiltration/buffer exchange and IMAC steps.

32. (Withdrawn) The method according to claim 1, wherein the AIE step is followed by a virus filtration step.

33. (Withdrawn) The method according to claim 1, where an AIE step utilising a weak anion exchange column is introduced between the IMAC and SEC steps.

34. (Withdrawn) An immunogenic variant of HER-2 protein that comprises the amino acid sequence set forth in SEQ ID NO: 2, residues 17-677.

35. (Withdrawn) The immunogenic variant of HER-2 protein according to claim 34 that consists of the amino acid sequence set forth in SEQ ID NO: 2, residues 1-677.

36. (Currently amended) A nucleic acid fragment that encodes an immunogenic variant of HER-2 protein that comprises the amino acid sequence set forth in SEQ ID NO: 2, residues 17-677 ~~the immunogenic variant of HER-2 protein according to claim 34 or 35~~.

37. (Original) The nucleic acid fragment according to claim 36, which is a

DNA fragment.

38. (Currently Amended) A vector carrying the nucleic acid fragment according to claim ~~36 or~~ 37.

39. (Original) The vector according to claim 38 ~~37~~, which is capable of autonomous replication.

40. (Currently Amended) The vector according to claim ~~37 or~~ 39 being selected from the group consisting of a plasmid, a phage, a cosmid, ~~a mini-chromosome,~~ and a virus.

41. (Currently Amended) The vector according to claim 38 ~~37~~, which is an expression vector.

42. (Currently Amended) The vector according to claim 41, comprising in the 5' → 3' direction and in operable linkage, a promoter for driving expression of the nucleic acid fragment according to claim ~~36 or~~ 37, ~~optionally~~ a nucleic acid sequence encoding a leader peptide enabling secretion of or integration into the membrane of the polypeptide fragment, and the nucleic acid fragment according to claim ~~36 or~~ 37~~, and optionally a nucleic acid sequence encoding a terminator~~.

43. (Previously Presented) A transformed host cell carrying the vector of claim 38 ~~37~~.

44. (Currently Amended) A stable cell line which carries the vector according to claim 41 ~~or 42 and which expresses the nucleic acid fragment according to claim 36 or 37, and which optionally secretes or carries the immunogenic variant of HER-2 protein according to claim 34 or 35 on its surface~~.

45. (Withdrawn) An immunogenic composition for immunizing against HER-2

protein in a human comprising the immunogenic variant of HER-2 protein according to claim 34 or 35 in admixture with a pharmaceutically acceptable carrier or vehicle and optionally an adjuvant.

46. (Currently amended) An immunogenic composition for immunizing against HER-2 protein in a human comprising the vector according to claim 41 ~~or 42~~ in admixture with a pharmaceutically acceptable carrier or vehicle and optionally an adjuvant.

47. (Withdrawn) A method for immunizing a human against autologous HER-2, the method comprising administering an immunogenically effective amount of

- the immunogenic variant of HER-2 protein according to claim 34 or 35, or
- the immunogenic composition according to claim 45, or
- the vector according to claim 41 or 42, or
- the immunogenic composition according to claim 46, to the human being.

48. (Withdrawn) The method according to claim 47 wherein the immunization against autologous HER-2 protein is used for treating or ameliorating cancer.

49. (Withdrawn) The method according to claim 20, wherein said fatty acid ester is a member selected from the group consisting of Tween 20, Tween 40, Tween 60, Tween 80 and Tween 85, said alkylaryl polyether alcohol is Triton X100, and said carbohydrate detergent is octylglycoside.

50. (Withdrawn) The method according to claim 22, wherein said divalent metal ion is Zn2+.

51. (Withdrawn) The method according to claim 24, wherein said concentration of imidazole is about 200 mM and said concentration of histadine is

about 100 mM.

52. (Withdrawn) The method according to claim 26, wherein said pH is about 7.5

53. (Withdrawn) The method according to claim 28, wherein said phosphate concentration is adjusted to between 10 and 12.5 mM.

54. (New) A nucleic acid fragment that encodes an immunogenic variant of HER-2 protein that consists of the amino acid sequence set forth in SEQ ID NO: 2, residues 17-677.